CASE REPORT

Iatrogenic magnesium toxicity following intravenous infusion of magnesium sulfate: risks and strategies for prevention

Gillian F Cavell,¹ Catherine Bryant,² Seetal Jheeta³¹King's College Hospital, London, UK²Department of Clinical Gerontology, King's College Hospital NHS Foundation Trust, London, UK³Imperial College Healthcare NHS Trust, London, UK**Correspondence to**Gillian F Cavell,
gillian.cavell@nhs.net

Accepted 2 July 2015

SUMMARY

A 65-year-old man being treated with radiotherapy and chemotherapy for recurrent colonic adenocarcinoma was admitted for management of hypokalaemia and hypomagnesaemia secondary to diarrhoea. He was treated with intravenous infusions of potassium chloride and magnesium sulfate. Following an infusion of magnesium sulfate, he experienced a sudden neurological deterioration. A CT of the head revealed no haemorrhage or evidence of acute ischaemic injury. Results of serum biochemistry later that day revealed an elevated magnesium level. Iatrogenic magnesium toxicity was suspected. Further discussions between the pharmacist and ward staff confirmed that a medication error had been made in the preparation of the infusion resulting in an overdose of intravenous magnesium.

BACKGROUND

Iatrogenic magnesium sulfate toxicity associated with eclampsia treated with intravenous infusions of magnesium sulfate has been well described in obstetric and anaesthesia journals.^{1–5} There is little information about magnesium toxicity outside obstetric settings, where lower doses of intravenous magnesium are used, for example, for magnesium supplementation.^{6,7}

Errors in the preparation of intravenous infusions are difficult to detect and may not be considered when the clinical condition of the patient changes. The preparation of infusions of magnesium sulfate may be prone to error due to the expression of concentration as %w/v, mmol/mL and g/mL on ampoules of concentrated magnesium sulfate solutions, which can cause confusion with drug dose calculation.⁸

We present this case to highlight the need for awareness of the potential for magnesium toxicity in patients receiving intravenous magnesium in general medical or surgical wards where it is prescribed and administered to treat hypomagnesaemia, and the importance of monitoring of serum magnesium levels in patients receiving intravenous magnesium who experience signs of neurological deficit.

CASE PRESENTATION

A 65-year-old man was referred to a hospital for the management of hypokalaemia.

The patient had a history of Dukes B rectal adenocarcinoma for which he had undergone an

anterior resection in February 2009. Recurrence was diagnosed by sigmoidoscopy in August 2012.

At the time of his admission, the patient was undergoing a course of chemoradiotherapy. He was experiencing significant diarrhoea, which had been worsening over the course of the treatment. He was passing very loose stools three to four times a day, and described being in pain and feeling fatigued. He had been prescribed loperamide to be taken after every loose bowel motion.

INVESTIGATIONS

Serum biochemistry prior to admission revealed hypokalaemia (serum potassium of 2.5 mmol/L; normal range 3.5–5.0 mmol/L) and hypophosphataemia (0.72 mmol/L; normal range 0.8–1.4 mmol/L). There was no evidence of renal impairment.

The patient was prescribed intravenous fluid replacement with two infusions of sodium chloride 0.9% (1000 mL) with 40 mmol potassium chloride over the next 14 h. Oral potassium supplements as effervescent potassium tablets were prescribed in a dose of 24 mmol three times daily.

At 00:45 on day 2 of his admission he remained hypokalaemic with a serum potassium of 2.7 mmol/L and his serum magnesium was 0.45 mmol/L (normal range 0.7–1.0 mmol/L) as shown in [table 1](#).

In response, the patient was initially prescribed oral magnesium glycerophosphate 12 mmol twice daily to treat hypomagnesaemia. Oral electrolyte supplementation would not have been effective due to continuing diarrhoea, so the patient was prescribed intravenous magnesium sulfate. An infusion of 12 mmol magnesium sulfate in 250 mL sodium chloride 0.9% over 4 h was prescribed at 07:20 on day 2 with the instruction to review magnesium levels after the infusion.

The infusion was prepared and administered on the ward by two nurses according to hospital policy at 08:35 on day 2. As the patient was scheduled to be transferred to another nearby hospital for his radiotherapy appointment, the duration of the infusion was decreased to 2 h so that it would finish before he was scheduled for transport. During the infusion, the patient reported of feeling lightheaded and had described a heavy feeling in his arms earlier that morning to his wife when she was visiting.

At 12:09 while being prepared for transfer, the patient suddenly became unwell with slurred speech and a reduced Glasgow Coma Scale score of 12/15. He did not report of any headache,

CrossMark

To cite: Cavell GF, Bryant C, Jheeta S. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-209499

Table 1 Serum biochemistry showing significant hypomagnesaemia

Serum biochemistry			
Day of admission		Day 1	Day 2
Time		07:35	00:45
Sodium	135–145 mmol/L	136	135
Potassium	3.5–5.0 mmol/L	2.6	2.7
Creatinine	45–120 µmol/L	60	53
Urea	3.3–6.7 mmol/L	7.2	5.8
Phosphate	0.8–1.4 mmol/L	0.65	0.55
Calcium	mmol/L	1.9	1.71
Corrected calcium	2.15–2.6 mmol/L	2.04	1.93
Magnesium	0.7–1.0 mmol/L		0.45
eGFR		>90	>90

eGFR, estimated glomerular filtration rate.

dizziness, palpitations or chest pain. Capillary blood glucose was 7.2 mmol/L, temperature 37.3°C, blood pressure 106/50 mm Hg and heart rate 66 bpm. Oxygen saturation was reduced at 93% on air. Neurological examination found no cranial nerve deficit and no cerebellar signs. Movement in his upper limbs was normal but he was unable to move his lower limbs. Plantar reflexes were down-going. A differential diagnosis of stroke, cerebral metastases or seizure was made.

An urgent CT of the head was requested.

Over the next 2 h, the patient started to feel much better and was reviewed on the ward by the medical team. Blood results from earlier were checked. Results from a blood sample taken at 12:08 reported magnesium levels as 3.55 mmol/L. These are shown in [table 2](#).

It was noted then that earlier symptoms were consistent with magnesium toxicity. A medication error was suspected. After discussions between the nursing staff and the ward pharmacist it was established that the infusion had erroneously been prepared using 50 mL (five 10 mL ampoules) of magnesium sulfate 50% (2 mmol/mL) instead of 6 mL of magnesium sulfate 50%. The patient had therefore received 100 mmol (25 g) of magnesium intravenously over approximately 2 h instead of the prescribed 12 mmol (3 g).

DIFFERENTIAL DIAGNOSIS

- ▶ Stroke
- ▶ Seizures
- ▶ Cerebral metastases

TREATMENT

Advice on management was sought from the clinical toxicity database of the UK National Poisons Information Service. A single dose of 10 mL of calcium gluconate 10% was administered by slow intravenous injection to mitigate the effects of magnesium on cardiac muscle, although an ECG showed no changes.

OUTCOME AND FOLLOW-UP

The symptoms of magnesium toxicity resolved over the next 6 h. Ten hours after the administration of the infusion, the patient's magnesium level was 1.57 mmol/L and was within the normal range at 0.86 mmol/L the following day (day 3).

The incident was explained to the patient and his wife, who were reassured that the magnesium would be cleared by the kidneys and that long-term adverse effects of the error were unlikely.

DISCUSSION

Neuromuscular toxicity of magnesium sulfate manifests as diminished deep tendon reflexes, hypothermia, progressive muscle weakness including respiratory muscle weakness resulting in respiratory paralysis and coma. Effects on the cardiovascular system include hypotension, tachycardia followed by bradycardia, increased PR interval, QRS duration and QT interval, complete heart block and asystole.

There are a number of case reports of patient harm resulting from acute magnesium toxicity although it is rare.

A 10-fold overdose of magnesium resulting in muscle paralysis and QT-prolongation was described in a series of reports of intravenous medication errors made to a Poisons Centre in Germany. The patient had received 60 g magnesium over 6 h and made a full recovery.⁹ Two case reports from an emergency department in the USA describe the administration of 20 g of intravenous magnesium sulfate against prescriptions for 2 g. Both resulted in asystole. One patient recovered and was discharged from hospital but the other died.⁶ Another case report from a US emergency department describes the administration of 2 vials of magnesium sulfate solution each containing 25 g against a prescription for 2 g. The 73-year-old patient developed sinus bradycardia with first degree atrioventricular block and required admission to a coronary care unit but made a full recovery.⁷

Magnesium sulfate toxicity has been described where intravenous magnesium is prescribed for the prophylaxis of seizures

Table 2 Serum biochemistry before and after magnesium supplementation

Serum biochemistry						
Day of admission		Day 1	Day 2	Day 2	Day 2	Day 3
Time		07:35	00:45	12:08	17:48	11:30
Sodium	135–145 mmol/L	136	135	137	137	137
Potassium	3.5–5.0 mmol/L	2.6	2.7	2.9	3.1	3.3
Creatinine	45–120 µmol/L	60	53	54	62	55
Urea	3.3–6.7 mmol/L	7.2	5.8	4.7	5.0	5.4
Phosphate	0.8–1.4 mmol/L	0.65	0.55	0.39	0.24	0.57
Calcium	mmol/L	1.9	1.71	1.74	1.68	1.45
Corrected calcium	2.15–2.6 mmol/L	2.04	1.93	1.94	1.9	1.69
Magnesium	0.7–1.0 mmol/L		0.45	3.55	1.57	0.86
eGFR		>90	>90	>90	>90	>90

eGFR, estimated glomerular filtration rate.

in the obstetric setting. Cases of acute magnesium toxicity resulting in respiratory impairment,¹ cardiopulmonary arrest^{2 3} and neurological depression,⁴ have been published. Magnesium levels of 8.1³ and 8.6 mmol/L⁴ were observed. One database of 52 cases of magnesium sulfate toxicity from Canada includes seven women who either died or were permanently harmed.⁵

Magnesium sulfate infusion errors were identified in a study of medication administration errors in five adult intensive care units (ICUs) in the USA.¹⁰ In an ICU in the UK, magnesium sulfate, along with heparin, insulin, inotropes, sedatives, potassium chloride and antibiotics, is commonly involved in reported medication errors.¹¹

Analysis of infusions prepared in a UK critical care unit to determine variability in drug concentrations cited magnesium infusions as a problem. When comparing the concentration of magnesium solutions left in syringes after infusion with the concentration described on the label, 6 of 30 syringes were found to contain 4–5 times more magnesium than stated on the syringe label. It was proposed that this was due to confusion between the dose expressed in millimoles and grams and the difficulty some practitioners have converting between the two resulting in an error in the preparation of the infusion at ward level.

Recently, the UK National Reporting and Learning System received a report of a harmful patient safety incident following the administration of a magnesium infusion containing 10 times more than the intended dose.¹²

Magnesium is a high-risk drug and errors in intravenous dose preparation and administration resulting in serious patient harm or death are described. However, these reports are infrequent possibly because these errors are undetected.

In this case, because magnesium levels were checked within hours of the magnesium infusion finishing, the toxic magnesium level was detected. Had the blood sample not been taken until later that day or the following morning, magnesium toxicity as a cause of the neurological changes may not have been considered. The patient may have been subjected to further unnecessary neurological investigations, which would not have confirmed the cause of the symptoms he experienced.

Inspection of empty infusion containers is unlikely to indicate deviations from prescribed doses. In this case, the infusion container of 250 mL sodium chloride 0.9% was labelled to indicate that 12 mmol magnesium sulfate had been added. This is what was prescribed and is what the nurses preparing the infusion intended to add, and believed they had added, to the infusion container. Only on direct questioning was the error in dose preparation identified.

Guidelines

For prescribers, the British National Formulary expresses magnesium dose in millimoles for hypomagnesaemia and in grams for the prevention of seizures in preeclampsia. For intravenous administration, the concentration of solutions is referred to as percentages and labels include additional information on the concentration of magnesium in grams/10 mL, mmol/mL or mmol/10 mL. There are therefore several different numbers which potentially could lead to dosing confusion.

We identified the labelling of magnesium sulfate 50% ampoules as a potential contributory factor in this case. At the time of this incident, the label on the ampoules and the label on the box specified the total amount of magnesium sulfate in each ampoule as 5 g in 10 mL, approximately 2 mmol Mg²⁺/mL. It is possible that this was interpreted as 2 mmol in 10 mL, although if this was the only cause of the error 6 ampoules (60 mL)

Figure 1 Labelling of magnesium sulfate 50% ampoules showing the change in specification of concentration to include 20 mmol/10 mL.

would have been used to prepare an infusion containing 12 mmol. We notified the manufacturer of the error and recommended that the labelling be reviewed to specify the total number of millimoles in each ampoule. This information is now included on the label, which specifies 2 mmol Mg²⁺/mL (20 mmol in 10 mL) (figure 1).

In the absence of ready to administer infusions of magnesium sulfate, a consistent approach to the labelling of concentrated magnesium solutions should be adopted to reduce the risk of accidental toxicity.

Patient's perspective

- ▶ I first realised that something was wrong when I began to feel an intense feeling of heat and pressure spreading throughout my body, seemingly towards my head.
- ▶ I called for help and immediately a whole team of medical staff were attending to me and asking me questions ("Do you know where you are Mr XXX?"). At this time I experienced two prominent symptoms: I was unable to raise my arms above shoulder height and also I experienced a slurring of speech.
- ▶ Soon after I slept and awoke with no further symptoms. I have since met with the staff concerned and accepted their apologies for the incident with an understanding that there are no long term effects.
- ▶ Clearly there is a serious issue which needs to be addressed by the senior staff involved to ensure that patients do not suffer as a consequence of inadequate administrative systems.

Learning points

- ▶ Magnesium toxicity should be suspected in any patient experiencing symptoms of neurological toxicity during or after administration of intravenous magnesium sulfate.
- ▶ Magnesium levels should be checked immediately if toxicity is suspected and should routinely be rechecked on completion of infusions.
- ▶ Calcium gluconate 10% should be administered to any patient with magnesium toxicity to reduce the risk of cardiac arrhythmia.
- ▶ Prescribing and administration guidelines for the treatment of hypomagnesaemia with intravenous magnesium sulfate should be standardised and include instructions for the preparation of infusions.
- ▶ Ideally, commercially manufactured, licensed, ready to administer solutions should be used for all doses of intravenous magnesium sulfate to eliminate the need for infusion preparation at ward level.

Contributors GFC conceived the idea of the report. GFC, SJ and CB made substantial contributions to the drafting and critiquing of the content of the report; and approved the final draft of the report.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 McDonnell NJ, Muchatuta NA, Paech MJ. Acute magnesium toxicity in an obstetric patient undergoing general anaesthesia for caesarean delivery. *Inj J Obstet Anesth* 2010;19:226–31.
- 2 Swartjes JM, Schutte MF, Bleker OP. Management of eclampsia: cardiopulmonary arrest resulting from magnesium sulphate overdose. *Eur J Obstet Gynaecol Reprod Biol* 1992;47:73–5.
- 3 Morisaki H, Yamamoto S, Morita Y, *et al.* Hypermagnesaemia-induced cardiopulmonary arrest before induction of anaesthesia for emergency caesarean section. *J Clin Anaesth* 2000;12:224–6.
- 4 Kumar K, Al Arebi A, Singh I. Accidental intravenous infusion of a large dose of magnesium sulphate during labour: a case report. *J Anaesthesiol Clin Pharmacol* 2013;29:377–9.
- 5 Simpson KR, Knox GE. Obstetrical accidents involving intravenous magnesium sulphate. Recommendations to promote patient safety. *Am J Matern Child Nurs* 2004;29:161–71.
- 6 Vissers RJ, Purcell R. Iatrogenic magnesium overdose: two case reports. *J Emerg Med* 1996;14:187–91.
- 7 Frohna WJ. Iatrogenic magnesium overdose in a patient with suspected acute myocardial infarction. *Am J Emerg Med* 1995;13:436–7.
- 8 Wheeler DW, Degnan BA, Sehmi JS, *et al.* Variability in the concentrations of intravenous drug infusions prepared in a critical care unit. *Intensive Care Med* 2008;34:1441–7.
- 9 Deters M, Prasa D, Hentschel H, *et al.* Iatrogenic intravenous medication errors reported to the GIZ-Nord Poisons Centre Gottingen. *Eur J Intern Med* 2009;20:728–31.
- 10 Calabrese AD, Erstad BL, Brandl K, *et al.* Medication administration errors in adult patients in the ICU. *Intensive Care Med* 2001;27:1592–8.
- 11 Mahajan RP. Medication errors: can we prevent them? *Br J Anaesth* 2011;107:3–5.
- 12 Medication Incident Review Panel 30th April 2014 <http://www.patientsafetyfirst.nhs.uk/Community/UserFiles/Default.aspx> (accessed Aug 2014).

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow